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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Macquarie Research Limited; Unisearch Limited
Serial No.	:	09/367,009
Filed	:	November 8, 1999
Title	:	Diagnosis of disease using tears
Examiner	:	M. Davis
Group Art Unit	:	1642

DECLARATION UNDER 37 C.F.R. § 1.132

I, GARY COBON, declare and say as follows:-

1. I am Director of the Australian Proteome Analysis Facility, Macquarie University, New South Wales, Australia, employed by Macquarie Research Limited, Macquarie University, New South Wales, Australia. A copy of my Curriculum Vitae including a list of my publications, is attached hereto and marked "Annexure A".

2. I have read and am thoroughly familiar with patent application serial No. 09/367,009 (hereinafter referred to as "the application"). Further, I have read and am thoroughly familiar with the Office Action mailed September 9, 2001. I am making this Declaration in support of the pending claims 1, 3 and 6 to 9.

3. The application discloses as its invention a method for screening or detecting cancer in an animal by detecting the presence of a protein having an N-terminal amino acid sequence as shown in SEQ ID NO: 3.

4. The Examiner has indicated that the claimed method lacks utility because the observation that SEQ ID NO:3 is similar to another protein, mammaglobin (now termed mammaglobin 1 or mammaglobin A) which is known to be expressed in malignant tissue is not sufficiently predictive of the function of a protein comprising

SEQ ID NO: 3. Consequently, the Examiner appears to consider that there is no support for the asserted utility.

5. However, I have carried out confirmatory experiments using human subjects which demonstrate that the presence in tears of a protein comprising SEQ ID NO: 3 correlates strongly with the presence of a malignant condition.

6. 28 patients from the Prince of Wales Hospital Oncology Day Centre, Barker Street, Randwick, New South Wales, Australia, were studied. 8 patients had breast cancer, 6 patients had lung cancer, 5 patients had colon cancer, 3 patients had ovarian cancer and 1 patient had prostate cancer. Of the remaining 5 patients, who were controls, 2 had a family history of cancer. The medical history of the cancer patients is attached hereto and marked "Annexure B".

7. Tears were collected from the patients using glass microcapillary tubes and frozen at −80°C. Tear samples were then analysed using 2D gel electrophoresis.

8. The protein spot volume of a protein comprising SEQ ID NO: 3 (hereinafter referred to as "lacryglobin") and a reference protein lipocalin were calculated for all samples using Melanie 2D software image analysis. The level of lacryglobin was expressed as a % ratio of lacryglobin over lipocalin to allow comparison between gels and tear samples. The ratio for each cancer patient is shown in Annexure B in the column marked "lacryglobin/lipocalin volume".

9. A summary of the frequency of lacryglobin detection in tear samples is attached hereto and marked "Annexure C". From this table it can be seen that the majority of cancer patients and controls with a family history of cancer showed the presence of lacryglobin in their tears as compared with the controls who had no family history of cancer.

10. Consequently, I consider that the detection of lacryglobin in tear samples is likely to be a useful, non-invasive means to screen for predisposition to, or the presence of, cancer in a patient.

11. With reference to the Examiner's comments on the unreliability of sequence comparisons, I would like to draw the Examiner's attention to a paper by another group of researchers, other than the inventors for the present application, who also

cloned a protein comprising the sequence shown as SEQ ID NO:3. Becker et al., 1998, Genomics 54: 70-78 (attached hereto and marked "Annexure D") designated their clone mammaglobin B on the basis of 58% identity with mammaglobin and the presence of conserved residues characteristic of the uteroglobin family. Consequently, both the inventors for the present application and an independent group came to the same conclusion with respect to the identity of the protein comprising the sequence shown as SEQ ID NO:3. This illustrates that although sequence identity on its own may not be enough to provide a satisfactory indicator of biological function, scientists tend to take other factors in account such as the presence of particular conserved motifs and the resulting predictions are routinely accepted in the art.

12. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further, that these statements are made with the knowledge that wilful false statements and the like are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such wilful false statements may jeopardise the validity of this application or any patent issuing thereon.

DECLARED at Sydney this 8th day of February 2002

GARY COBON